Welcome to the CLU-IN Internet Seminar

Arsenic - Health and Remediation Applications, Session 1
Sponsored by: NIEHS Superfund Research Program
Delivered: October 19, 2012, 2:00 PM - 4:00 PM, EDT (18:00-20:00 GMT)

Instructors:
William Suk, Ph.D., director, Superfund Research Program (suk@niehs.nih.gov)
Joseph H. Graziano, Ph.D., program director Columbia University SRP Center (jg24@columbia.edu)
Margaret Karagas, Ph.D., Dartmouth College SRP Center (Margaret.Karagas@Dartmouth.Edu)
A.Eduardo Sáez, Ph.D., University of Arizona SRP Center (esaez@email.arizona.edu)
Moderator:
Joseph H. Graziano, Ph.D., program director Columbia University SRP Center (jg24@columbia.edu)

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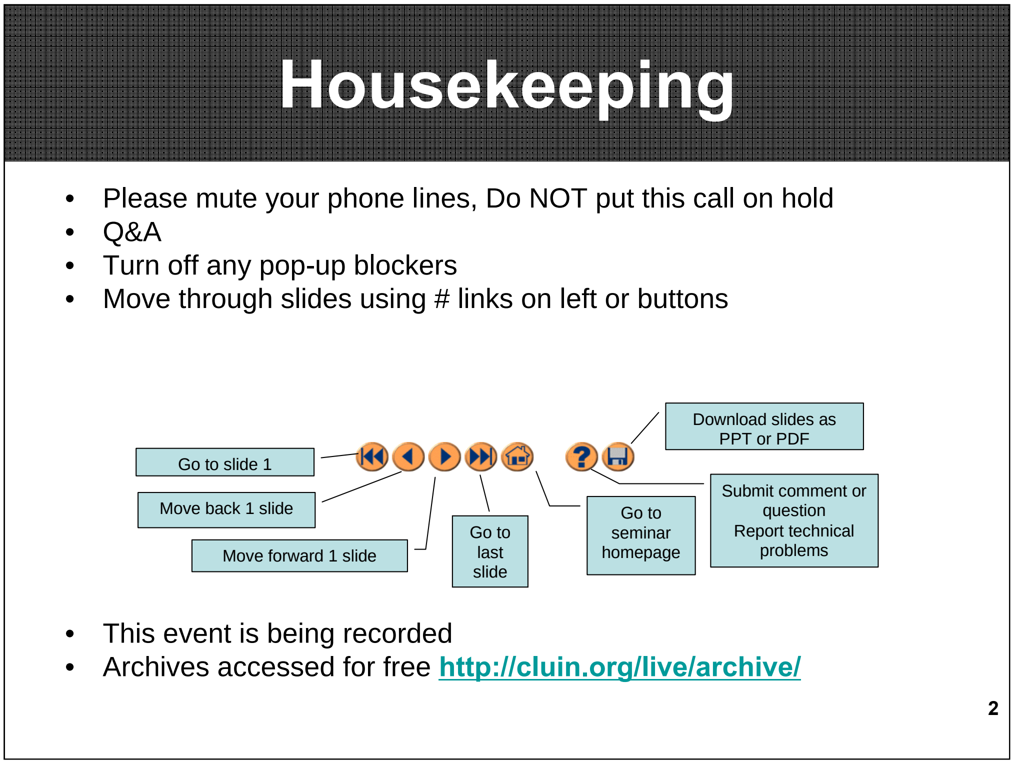

Although I'm sure that some of you have these rules memorized from previous CLU-IN events, let's run through them quickly for our new participants.

Please mute your phone lines during the seminar to minimize disruption and background noise. If you do not have a mute button, press *6 to mute #6 to unmute your lines at anytime. Also, please do NOT put this call on hold as this may bring delightful, but unwanted background music over the lines and interupt the seminar.

You should note that throughout the seminar, we will ask for your feedback. You do not need to wait for Q&A breaks to ask questions or provide comments. To submit comments/questions and report technical problems, please use the ? Icon at the top of your screen. You can move forward/backward in the slides by using the single arrow buttons (left moves back 1 slide, right moves advances 1 slide). The double arrowed buttons will take you to 1st and last slides respectively. You may also advance to any slide using the numbered links that appear on the left side of your screen. The button with a house icon will take you back to main seminar page which displays our agenda, speaker information, links to the slides and additional resources. Lastly, the button with a computer disc can be used to download and save today's presentation materials.

With that, please move to slide 3.

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Emerging Issues: Arsenic Exposure

Joseph H. Graziano, Ph.D.
Program Director
Columbia University Superfund Research Program

NIEHS Superfund Research Program
Health Effects and Geochemistry of Arsenic and Manganese
Columbia University

Superfund Research Program

NIH...Turning Discovery Into Health

Arsenic Presents a Major Public Health Problem

- Known carcinogen
  - Lung, liver, skin, bladder, kidney, and more
  - Early life exposure → increased risk as adults
- Multiple potential health effects on essentially every bodily system
  - Skin
  - Respiratory system
  - Cardiovascular system
  - Endocrine system (e.g., diabetes)
  - Immune system
  - Nervous system
  - And more…
- Arsenic rated #1 on the ATSDR 2011 Substance Priority List as the top chemical of concern as a public health hazard

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History of SRP Arsenic Research

- SRP has been committed to arsenic research since the inception of SRP in 1987
- SRP takes a “soup-to-nuts” approach to arsenic research and development
  - Detection systems
  - Remediation
  - Identifying and reducing exposures
  - Health effects
  - Training and education of scientists and community partners
  - Community and government engagement
  - Transdisciplinary partnerships to solve problems in communities

srp Superfund Research Program

NIEHS National Institute of Environmental Health Sciences

History of SRP Arsenic Research

- Started funding arsenic research from SRP's inception in 1987
- Currently funding numerous arsenic-related projects at 19 university SRP research centers
- SRP researchers have published over 150 arsenic-related scientific papers since 2006

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SRP Activities to Address Arsenic Challenges

- Identifying sources of contamination
- Characterizing toxic arsenic species and biomarkers of exposure in humans
- Identifying arsenic-related health effects and mechanisms of toxicity
- Exploring ways to mitigate health effects
- Engaging communities, government, and stakeholders as partners in solving real-life problems related to arsenic
- Training scientists in arsenic research

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Variable Toxicity of Arsenic Metabolites

		LD_{50} (Toxicity)
Inorganic Arsenic		
•As^{+3}	Arsenite	8 mg/kg
•As^{+5}	Arsenate	22 mg/kg
Mammalian Metabolites		
•MMA^{+3}	Monomethylarsonous Acid	**2 mg/kg**
•MMA^{+5}	Monomethylarsonic Acid	916 mg/kg
•DMA^{+5}	Dimethylarsinic Acid	648 mg/kg
Fish Metabolites		
•AsB	Arsenobetaine	~10,000 mg/kg
•AsC	Arsenocholine	

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What We Have Learned: Arsenic Exposure

- Naturally occurring element in Earth's crust
- Industrial sources (e.g., former smelters)
- Some types of chemically treated wood
- Some homeopathic remedies

- Drinking water
- Diet (e.g., rice)
- Soil and dust

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Arsenic in Groundwater: An International Problem

- Taiwan
- China
- Chile
- Argentina
- Mexico
- United States
- India
- Bangladesh
- Nepal
- Vietnam
- Cambodia
- Mongolia

U.S. EPA Maximum Contaminant Level for arsenic: 10 μg/L.

Concentrations reported in some regions of many of these countries reached over 3,000 μg/L.

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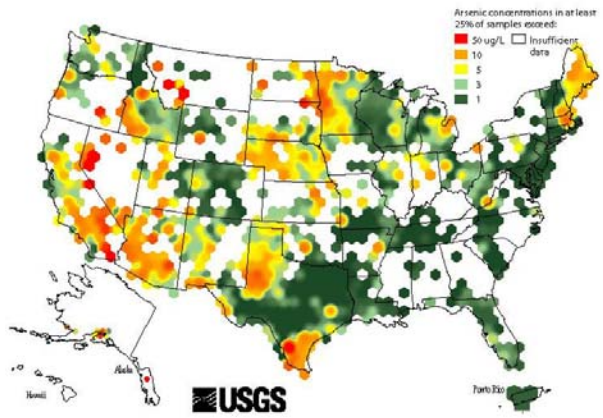
Arsenic in Groundwater in the U.S.



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Global and U.S. Activities Funded by NIEHS SRP

- **Large cohort studies**
  - Bangladesh
  - Chile
- **Global/U.S. studies of exposures and health effects**
  - Identify and reduce exposures
  - Identify health effects
  - Identify mechanisms of toxicity
  - Explore approaches to mitigating toxicity
- **Taking action at the local level**
  - Outreach to encourage private well testing
  - Helping provide safe water sources

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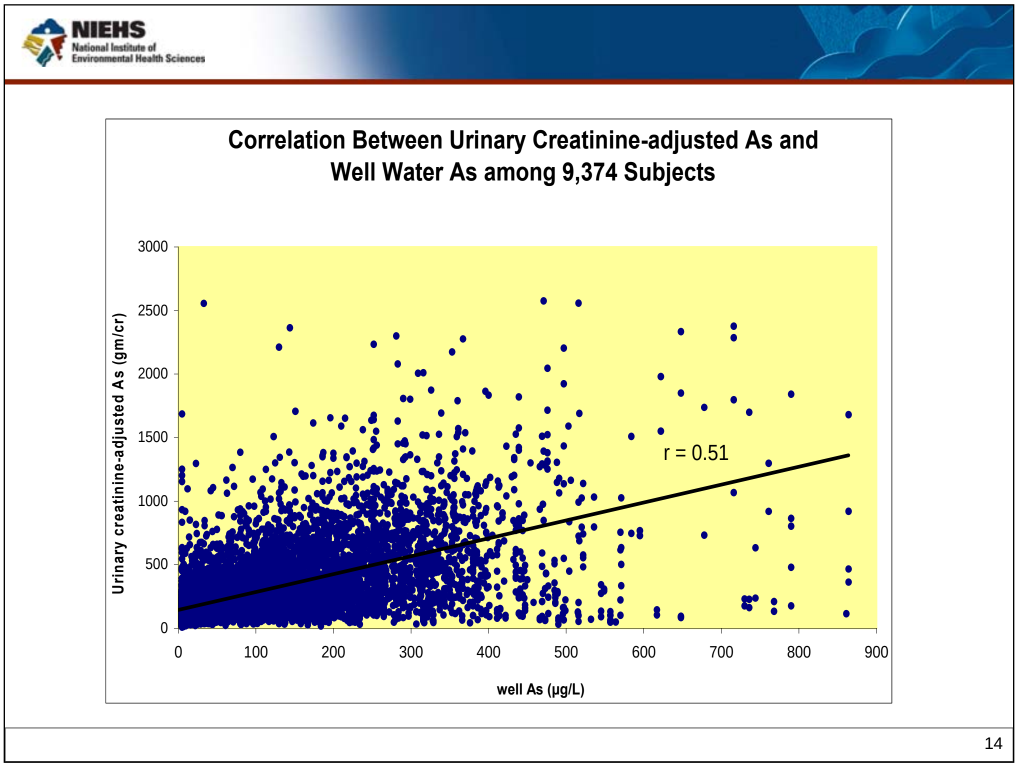
SRP-funded Cohort Studies

Health Effects and Longitudinal Study (HEALS) in Bangladesh

- Population exposed via tube wells
- Revealing information about exposure, health effects, susceptibilities, and nutritional factors

Chilean Cohort

- Population exposed for a defined period of time
- Population followed for >50 years
- Revealing information about health effects and latency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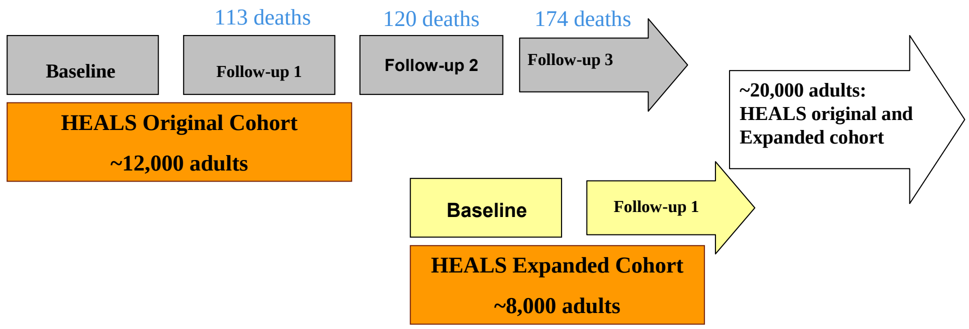
Correlation Between Urinary Creatinine-adjusted As and
Well Water As among 9,374 Subjects
Urinary creatinine-adjusted As (gm/cr)
well As (µg/L)
r = 0.51
0
500
1000
1500
2000
2500
3000
0
100
200
300
400
500
600
700
800
900

HEALS Cohort Recruitment and Follow-up



A validated verbal autopsy was used to classify deaths using WHO's ICD-10

All-cause and Chronic Disease Mortality

Table 2. Hazard ratio for mortality of HEALS participants in relation to baseline arsenic exposure, Bangladesh

Arsenic exposure	No. of deaths	All-cause mortality*		No. of deaths	Chronic disease mortality*	
		HR	95% CI		HR	95% CI
Well water arsenic (μg/L)						
0.1–10	74	1.00	Referent	58	1.00	Referent
10.1–50	90	1.34	0.99, 1.82	69	1.33	0.94, 1.87
50.1–150	98	1.09	0.81, 1.47	83	1.22	0.87, 1.70
150.1–854	131	1.68	1.26, 2.23	101	1.68	1.21, 2.33
P for trend		0.003			0.005	
Daily arsenic dose (μg/day)						
0.041–35.0	87	1.00	Referent	66	1.00	Referent
35.1–163.0	97	1.10	0.83, 1.47	80	1.21	0.88, 1.67
163.1–401.0	91	1.09	0.81, 1.46	76	1.22	0.88, 1.71
401.1–4898.0	118	1.54	1.17, 2.04	89	1.58	1.15, 2.18
P for trend		0.004			0.007	
Urinary total arsenic (μg/g Cr)						
7.0–105.0	83	1.00	Referent	64	1.00	Referent
105.1–199.0	96	1.07	0.80, 1.43	80	1.17	0.84, 1.62
199.1–352.0	100	1.22	0.91, 1.63	83	1.37	0.98, 1.90
352.1–5000.0	105	1.45	1.09, 1.94	77	1.47	1.05, 2.06
P for trend		0.008			0.01	

HR=hazard ratio; CI=confidence interval; Cr=creatinine.

* Multivariate estimates adjusted for age, sex, body mass index, systolic blood pressure, education, and smoking status.

Argos et al. 2010. Lancet 376: 252

Early Life Exposure Can Have Effects into Adulthood

- Increased infant mortality
- Reduced birthweight
- Increased infections during infancy and childhood
- Neurological and motor impairments in children
- Increased cancer risks as children (liver cancer)
- Increased cancer risks as adults (lung, bladder, and kidney cancer)

Vahter 2008.
Basic Clin Pharmacol Toxicol 102(2):204.

Early Life Exposure Can Have Life-long Effects

Increased Mortality from Lung Cancer and Bronchiectasis in Young Adults after Exposure to Arsenic *in Utero* and in Early Childhood

Allan H. Smith,[1] Guillermo Marshall,[2] Yan Yuan,[1] Catterina Ferreccio,[2] Jane Liaw,[1] Ondine von Ehrenstein,[1] Craig Steinmaus,[1,3] Michael N. Bates,[4] and Steve Selvin[4]

[1]Arsenic Health Effects Research Program, University of California, Berkeley, California, USA; [2]Pontificia Universidad Católica de Chile, Santiago, Chile; [3]Office of Environmental Health Hazard Assessment, California Environmental Protection Agency, Oakland, California, USA; [4]School of Public Health, University of California, Berkeley, California, USA

Environ Health Perspect 114:1293–1296 (2006).
doi:10.1289/ehp.8832 available via *ttp://dx.doi.org/*

SRP: Making a Difference in the Community

Columbia University SRP in Bangladesh

- Installation of >150 deep community wells that provide low-arsenic water to thousands of residents
- Providing primary medical care to the >20,000 HEALS participants

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Inter-School Art Contest

School-Based Educational Intervention in Araihazar, Bangladesh

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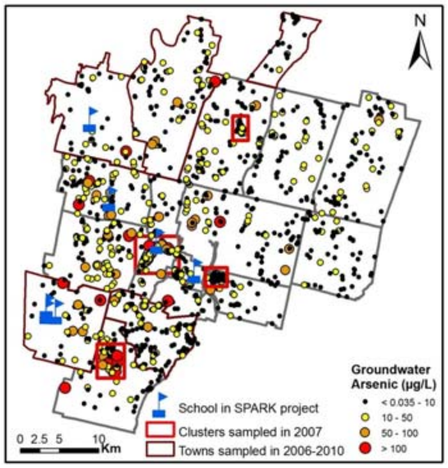
SRP: Making a Difference in the Community

Columbia University SRP in Maine

- Established a Community Engagement Core
- Disseminating knowledge about the hazards of local well water arsenic contamination
- Disseminating technologies to filter arsenic

Community Engagement in Maine



- Arsenic concentrations in 1,428 domestic wells from 17 towns central Maine
- 31% of the wells contain >10 ug/L arsenic (source: Yang 2010).
- Columbia Community Engagement Core aims to double the testing and treatment rate for arsenic in these towns. A survey is underway to determine the current rates.

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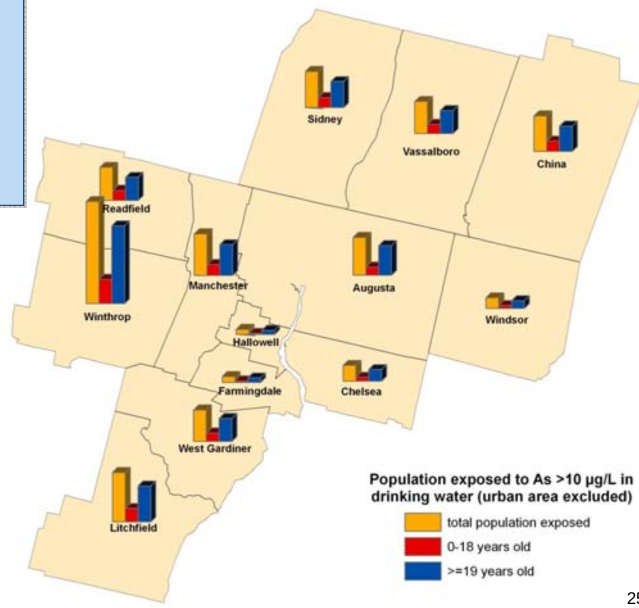
Assessment of Exposures to High Concentrations of Arsenic in Well Water in Maine



[As] >10 ug/L in Maine
Total Exposed = 12,458
0-18 yr olds = 3272
(2000 Census)

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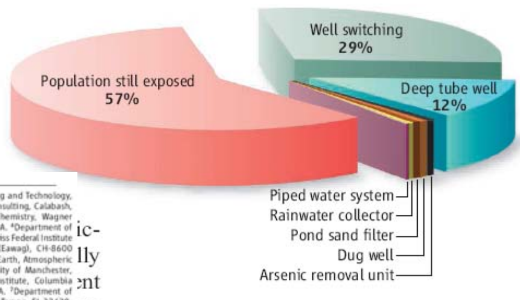
POLICYFORUM

EPIDEMIOLOGY

Ensuring Safe Drinking Water in Bangladesh

Excessive levels of arsenic in drinking water is a vast health problem in Southeast Asia. Several viable approaches to mitigation could drastically reduce arsenic exposure, but they all require periodic testing.

M. F. Ahmed,[1] S. Ahuja,[2] M. Alauddin,[3] S. J. Hug,[4] J. R. Lloyd,[5] A. Pfaff,[6] T. Pichler,[7] C. Saltikov,[8] M. Stute,[9,10] A. van Geen[10*]



[1]Bangladesh University of Engineering and Technology, Dhaka -1000, Bangladesh. [2]Ahuja Consulting, Calabash, NC 28467, USA. [3]Department of Chemistry, Wagner College, Staten Island, NY 10301, USA. [4]Department of Water Resources and Drinking Water, Swiss Federal Institute of Aquatic Science and Technology (Eawag), CH-8600 Duebendorf, Switzerland. [5]School of Earth, Atmospheric and Environmental Sciences, University of Manchester, Manchester M13 9PL, UK. [6]Earth Institute, Columbia University, New York, NY 10027, USA. [7]Department of Geology, University of South Florida, Tampa, FL 33620, USA. [8]Environmental Toxicology, University of California, Santa Cruz, Santa Cruz, CA 95064, USA. [9]Department of Environmental Sciences, Barnard College, Columbia University, New York, NY 10027, USA. [10]Lamont-Doherty Earth Observatory of Columbia University, Palisades, NY 10964, USA.

*Correspondence to: avangeen@ldeo.columbia.edu

ic- lly ent are he are to

Impact of arsenic mitigation in Bangladesh (SOM Text). The initially exposed population has been estimated at 28 to 35 million relative to the local standard of 50 µg per liter arsenic in drinking water (*3*).

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Bill Suk, NIEHS
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Atmospheric transport of metal and metalloid contaminants by dust and aerosol from mining operations

E.A. Betterton, J.C. Csavina, O. Felix, K. Rine, J. Field, M. Russell, M. Stovern, P. Saliba, M.P. Taylor, Scott White, Juliana Gil, Raina Meier, A.E. Sáez

Risk e-Learning Seminar, 19 October 2012


Mt. Isa, Australia


Hayden , AZ


Iron King tailings, Dewey-Humboldt, AZ

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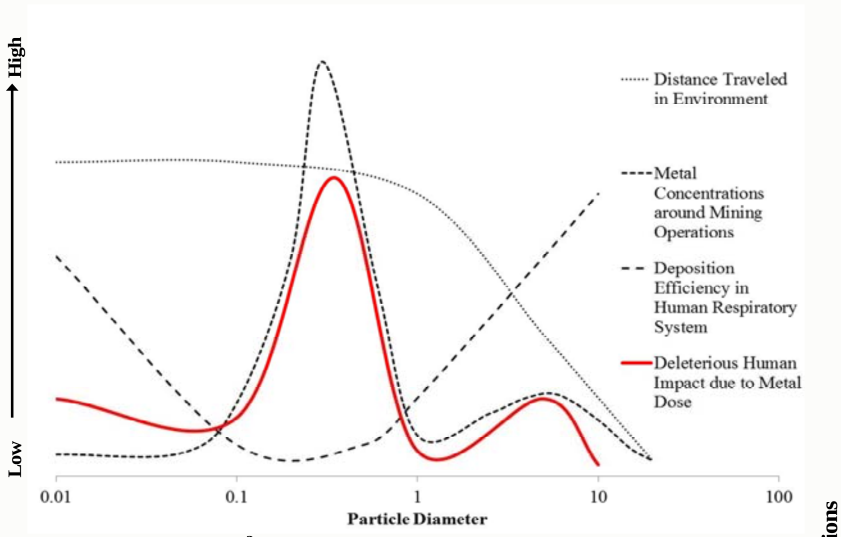
ARIZONA

Mining operations that generate dust and aerosol

- Crushing, grinding,
  mine tailings management
  - Coarse particles >2.5 µm
    mechanical action
    τ ≈ min to hours
- Smelting, Refining
  - Ultra-fine <0.1 µm
    gas - particle conversion
    τ ≈ sec to min
  - Accumulation 0.1-2.5 µm
    coagulation of ultrafine and condensation growth
    τ ≈ 10 days

Emissions from mining activities

Why do we care about mining operation particles?



$PM_{2.5}$: 35 μg/m³

PM_{10}: 150 μg/m³

Pb: 150 ng/m³

Methods

TSP (Total Suspended Particulate)

- Mass concentration for all ambient particulate

MOUDI (Micro-Orifice Uniform Deposit Impactor)

- Size fractioned aerosols in 11 different sizes ranging
  from 18 to 0.056 µm

Dusttrak Aerosol Monitor

- Optical mass measurements of aerosols

SMPS (Scanning Mobility Particle Sizer)

- Number concentration of aerosols <1 µm

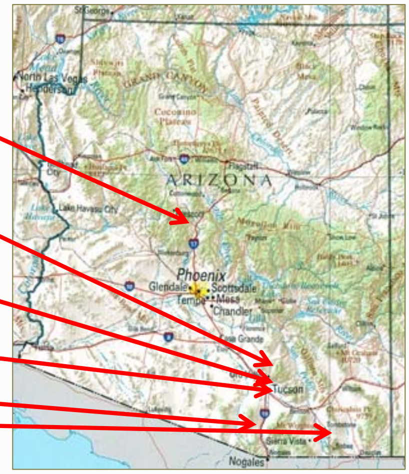
Weather Station

- Wind speed/direction, temperature, relative humidity

Metal and metalloid content: ICP-MS after extraction with *aqua regia*

Arizona Field Sites

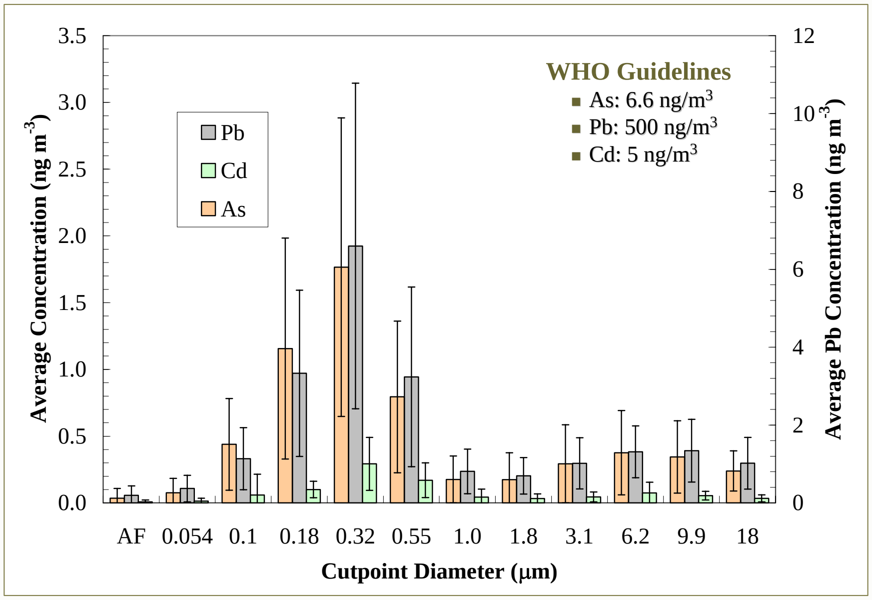
- **Contaminated Sites**
  - **Iron King** - Inactive copper mine and smelter; now a Superfund site (arsenic, lead contaminated tailings)
  - **Hayden & Winkelman** - ASARCO active copper mine with smelter (arsenic, lead contaminated soil; airborne lead)
- **Comparison Sites**
  - **Mount Lemmon** - Remote background
  - **Tucson** - Urban
  - **Green Valley** - Active copper mine; "clean" tailings
  - **Wilcox Playa** - Natural dust source

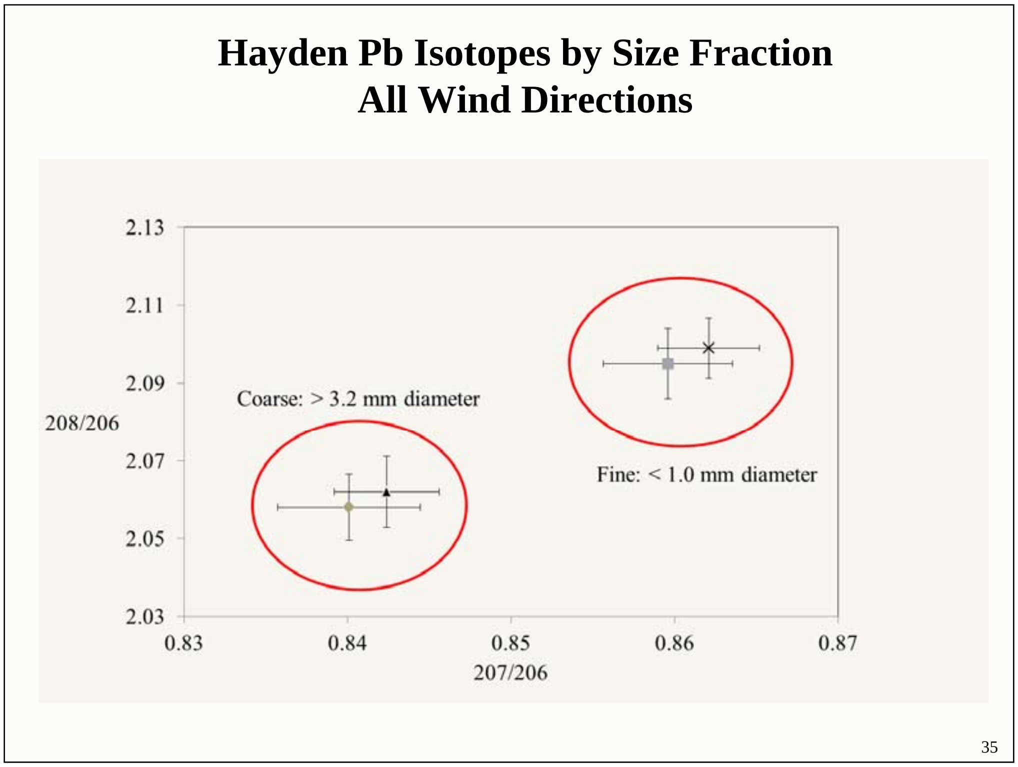


Australia Field Sites

- **Mount Isa, Qld Australia**
  XSTRATA Cu, Zn, Pb, and Ag mine with smelter
  2010/2011 airborne emissions:
  As =44,000 kg and Pb =160,000 kg
- **Port Pirie, SA Australia**
  Nystar Pb smelter
  2010/2011 airborne emissions:
  As =1,100 kg and Pb =44,000 kg
- **Sydney, NSW Australia**
  urban reference site

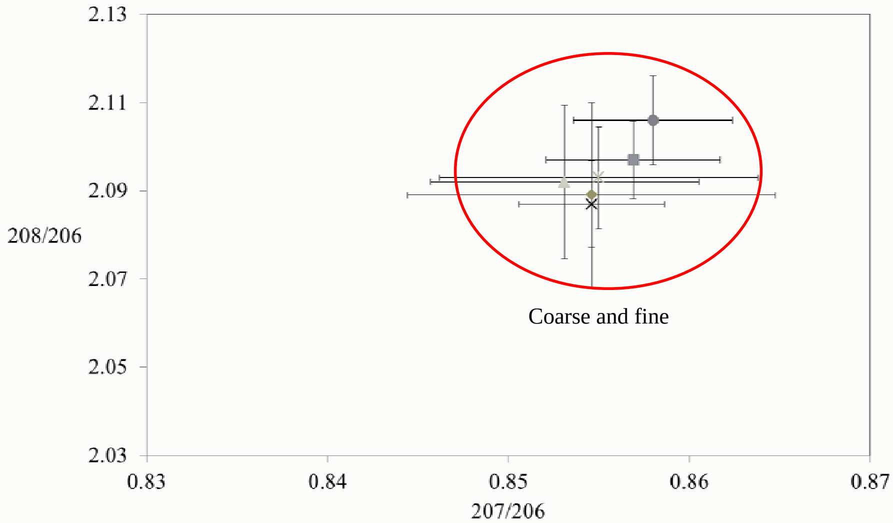
Hayden - MOUDI Results
2009 Annual Average



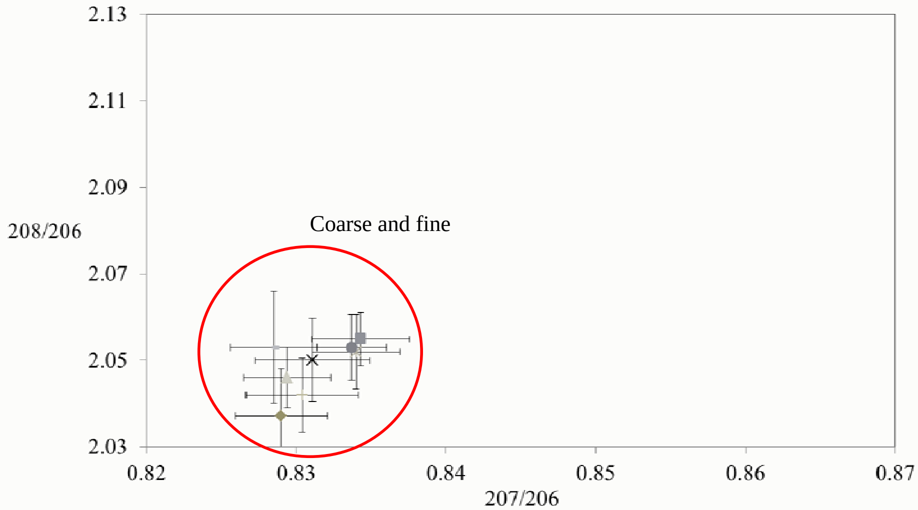


This graph shows that the isotope ratios are different for fine and coarse particles, it is known that smaller particles are related with process involving high temperatures, also in the literature was found that higher ratios are related with mining and smelting activities. From this graph we can conclude that the source of lead in fine and coarse particles is different, we have at least two sources.

Hayden Pb Isotopes by Size Fraction
Wind from Smelter

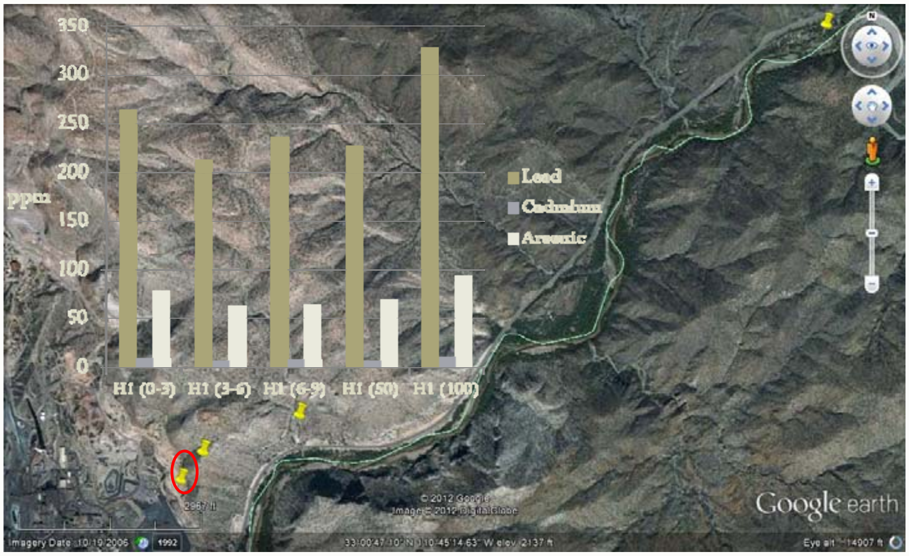


Tucson Pb Isotopes by Size Fraction



Contaminants in Soil - Hayden Site

Soil Concentrations 0.2 mi from smelter

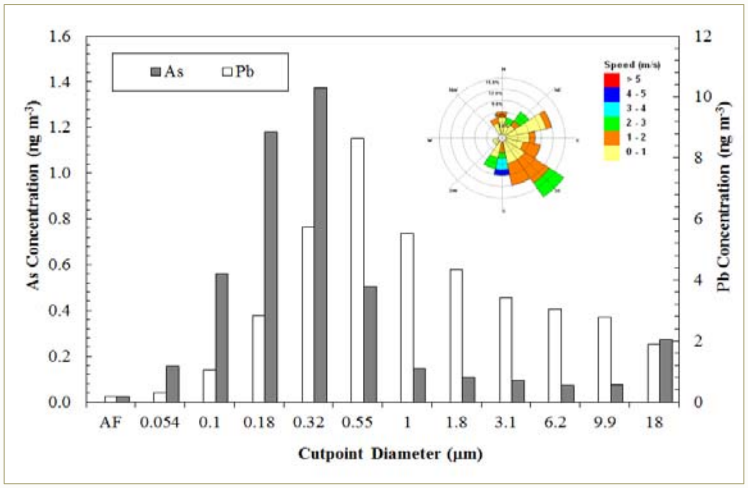


Soil Concentrations 0.8 mi from Smelter

Soil Concentrations 2.5 mi from Smelter

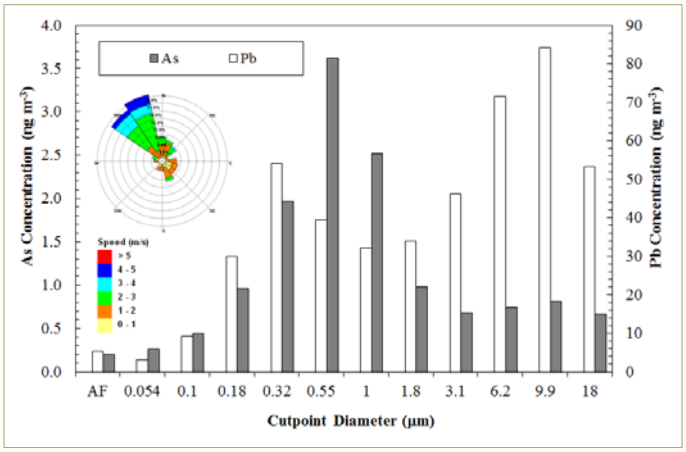
Mount Isa, Qld Australia
MOUDI Results

- 2 different maxima at 0.32 and 0.55 µm for As and Pb, respectively.
- Again majority of contaminants in fine size fraction. (average 75% <1 µm)



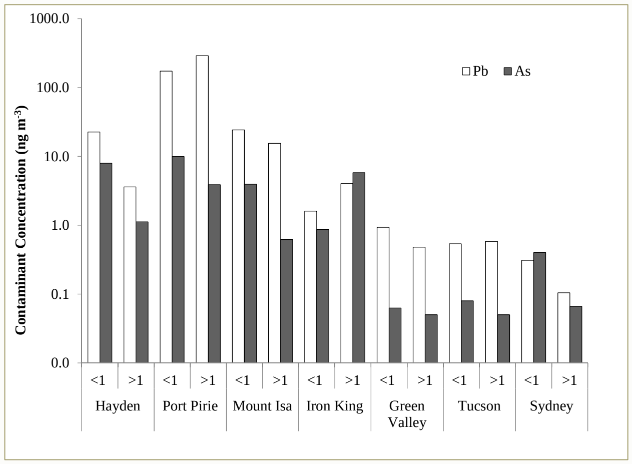
Port Pirie, SA Australia
MOUDI Results

- Both As and Pb follow bimodal distributions.
- Majority of As in fine size fraction.
- Particles have significant concentrations of Pb in the coarse size fraction likely due to crushing grinding operations of Pb ore.



MOUDI Field Site Comparison

- Concentrations summed over fraction with particles sizes <1 and >1 µm.
- Concentrations for As and Pb enriched in the fine size fraction around smelting operations except Port Pirie Pb concentrations.
- With windblown contaminated mine tailings as source, Iron King is more heavily impacted in the coarser size fraction.

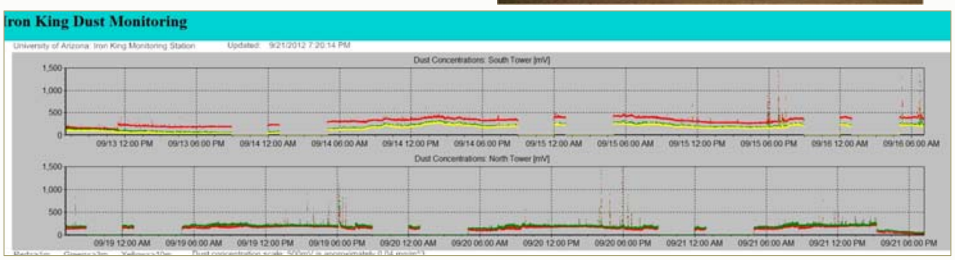


The Iron King Mine Humboldt Smelter Superfund Site

- Sulfide ore body discovered in 1880
- Operated 1904-1969; 3250 ft deep and 40 miles of shafts
- Lead, gold, silver, zinc, and copper mined
- Closed 1967
- Tailings pH = 2 to 4
- Tailings contain up to 4000 mg/kg arsenic
  up to 4000 mg/kg lead
- Listed as an NPL site in Sept. 2008

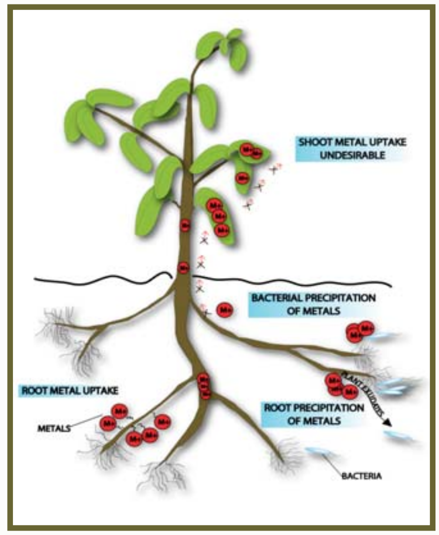
Iron King
Dust Flux Monitors

- Two 10-m dust flux towers
- PM_{10}, $PM_{2.5}$, $PM_{1.0}$
- Passive dust samplers
- Meteorological stations
- 3-D wind anemometer

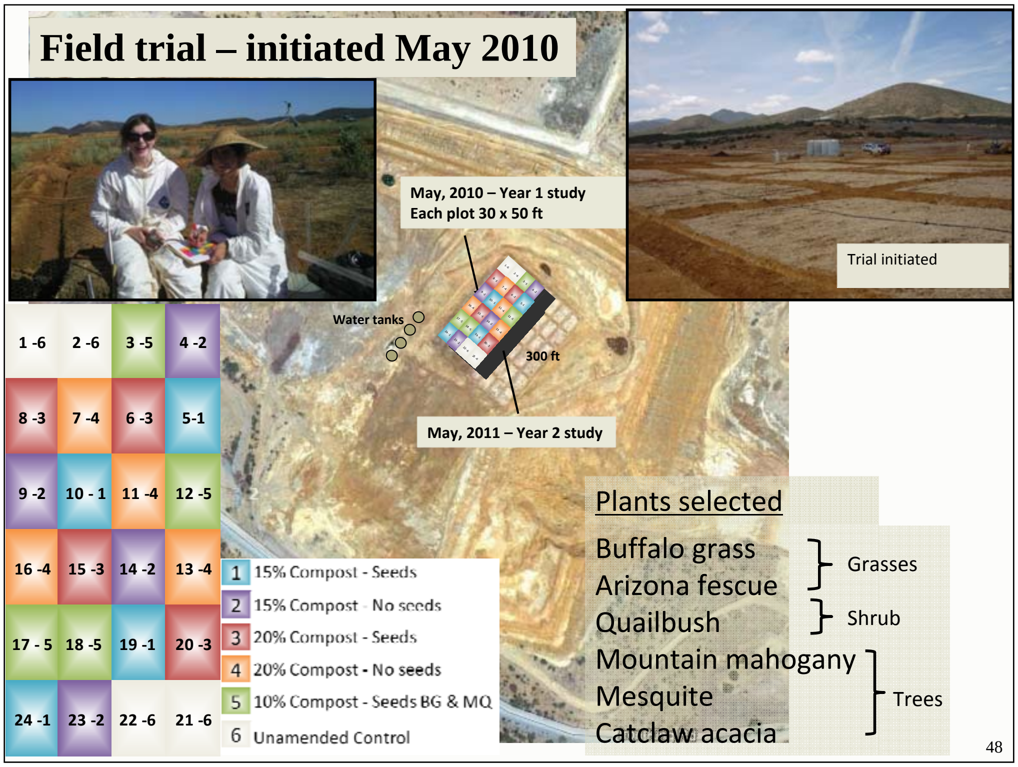


Direct Assisted Phytostabilization

- Stabilization of tailings by direct amendment (e.g., compost, lime) to allow establishment of drought-, salt-, and metal-tolerant plants.
- No soil cap used.
- Plants should not shoot-accumulate metals.
- Metal bioavailability (and hence toxicity) decreases as plants facilitate the precipitation of metals to less soluble forms, for example, metal sulfides or metal carbonates.



Mendez and Maier, 2008. Environ. Health Perspec.



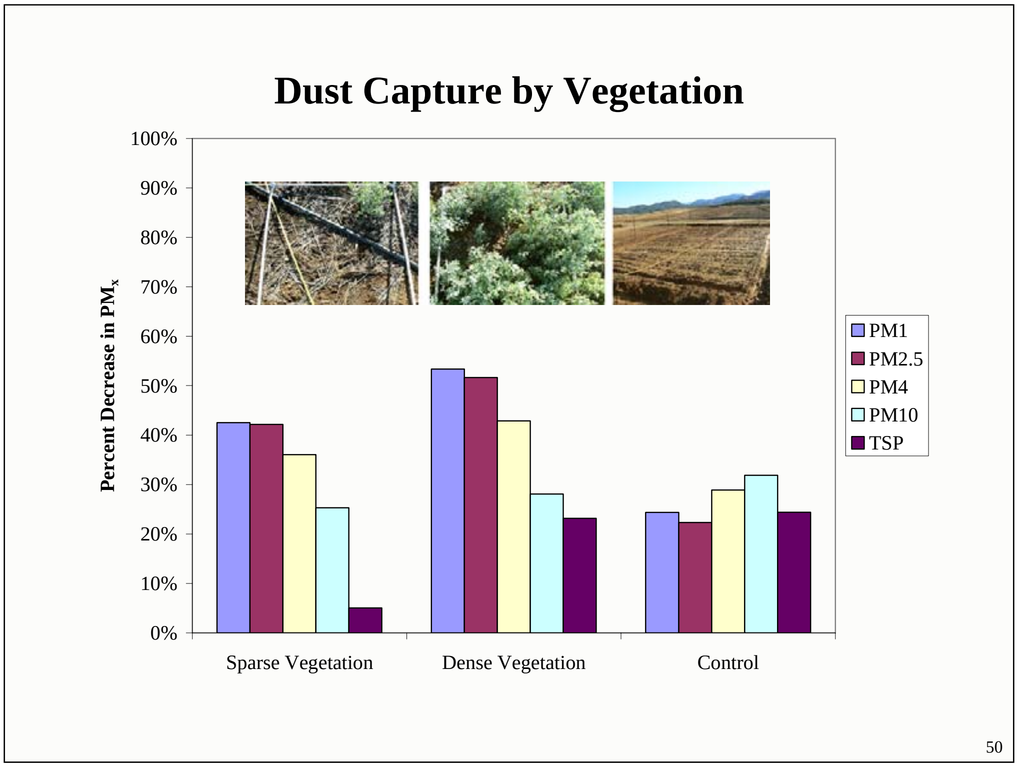
This figure explains the studies we are doing with TSPs and Dusttrak around the phytoremediation plots. We set the instruments up on either side of the plots as described above in the numbers. The windrose coincides with the sampling results in the following plot. The instruments were run for 4 hours. The Dusttrak samples continuously with optical measurements of mass concentrations of the different size fractions of particulate matter. TSP collects the ambient particulate on a filter which I have yet to get the metals results back. Future work includes duplicate studies like this and the passive samplers which are located throughout the plots to characterize horizontal dust flux.

Canopy Cover (measured at 5 and 16 months)

Treatments	--------- % Canopy Cover ----------		
	5 Months	16 Months	T-test
20% - Seeds	33.8 ± 5.4 a	32.8 ± 14.5 a	NS
15% - Seeds	38.7 ± 6.6 a	23.3 ± 19.5 ab	NS
10% - BG/MQ	29.9 ± 10.0 a	29.7 ± 18.6 ab	NS
Unamended control	0 b	0 b	NS

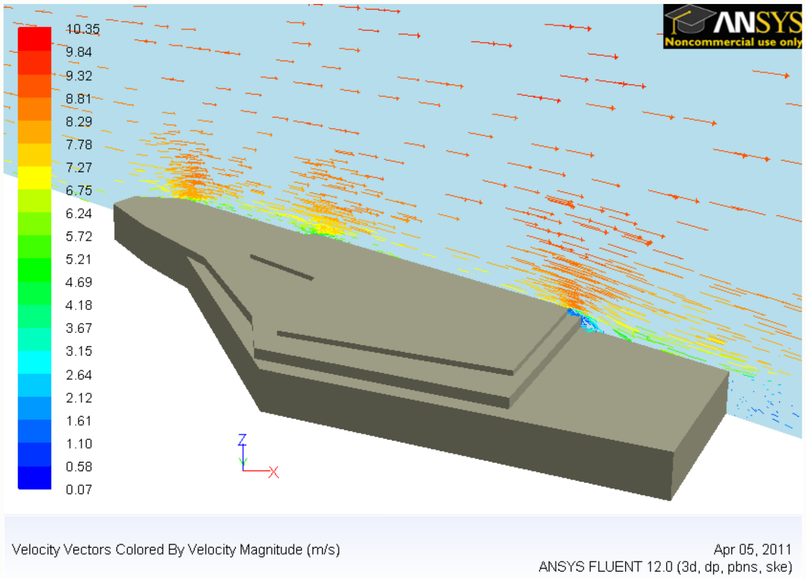
	0 - 5 mo	5 - 16 mo
Irrigation	37.8 cm	61.1 cm
Rainfall	32.8 cm	21.7 cm
Total	70.6 cm	82.8 cm

~ 30% canopy cover is equivalent to off-site vegetation



Dusttrak results for the percent decrease of PMx crossed the plots. This is one sampling period on 5/24/11. What might be happening with the coarser particles is that the plants are trapping them and then high winds are resuspending them. The finer particles are affect more by diffusive forces than wind force. So this is what we would expect to see.

CFD Modeling: IK Mine Tailings

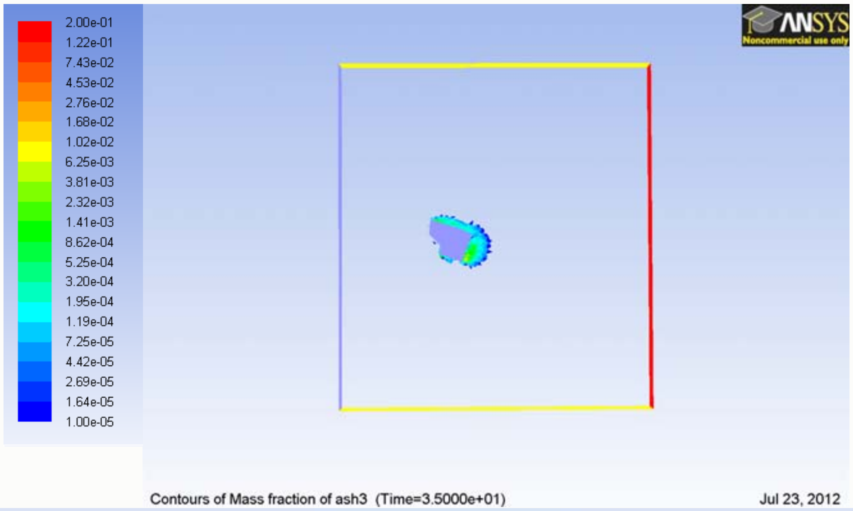


Simulated wind speeds over tailings

Mine tailings

Humboldt

Simulation of conservative tracer plume



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1.68e-02
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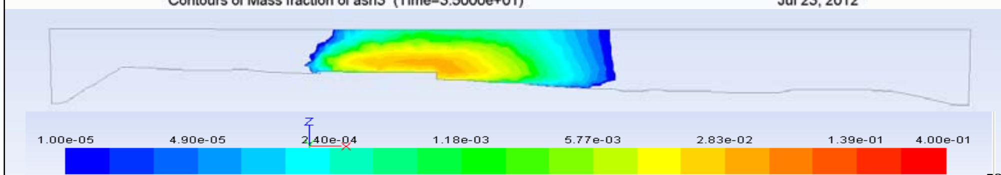
2.32e-03
1.41e-03
8.62e-04
5.25e-04
3.20e-04
1.95e-04
1.19e-04
7.25e-05
4.42e-05
2.69e-05
1.64e-05
1.00e-05
ANSYS
Noncommercial use only
Contours of Mass fraction of ash3 (Time=3.5000e+01)
Jul 23, 2012



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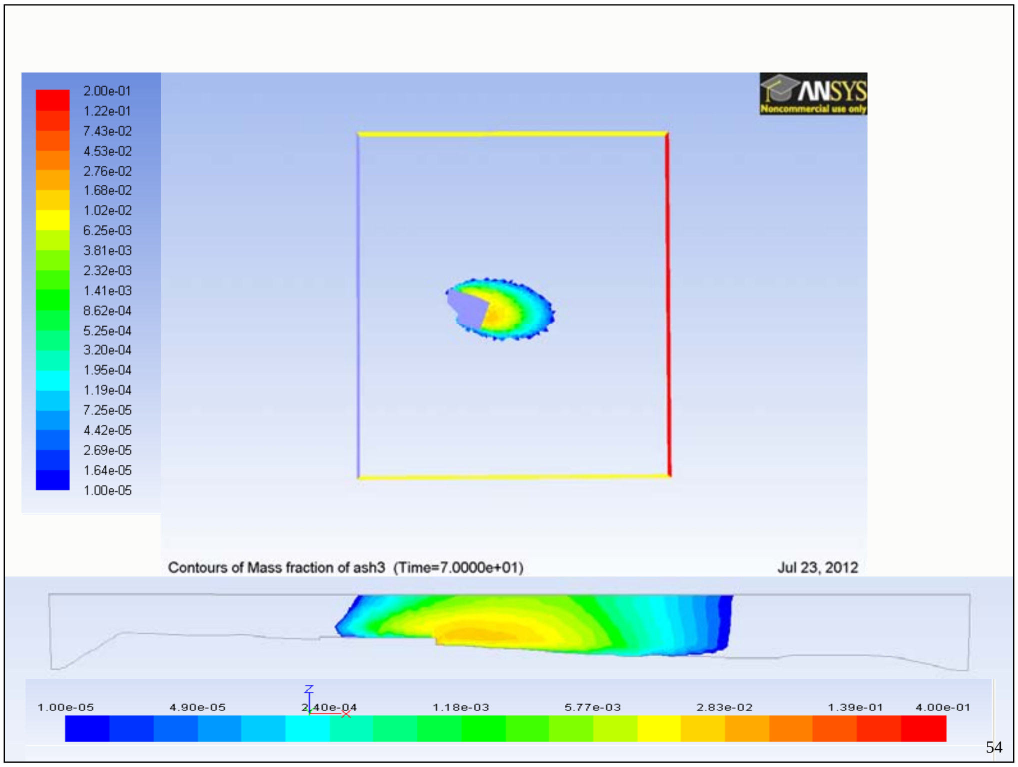
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ANSYS
Noncommercial use only
Contours of Mass fraction of ash3 (Time=7.0000e+01)
Jul 23, 2012
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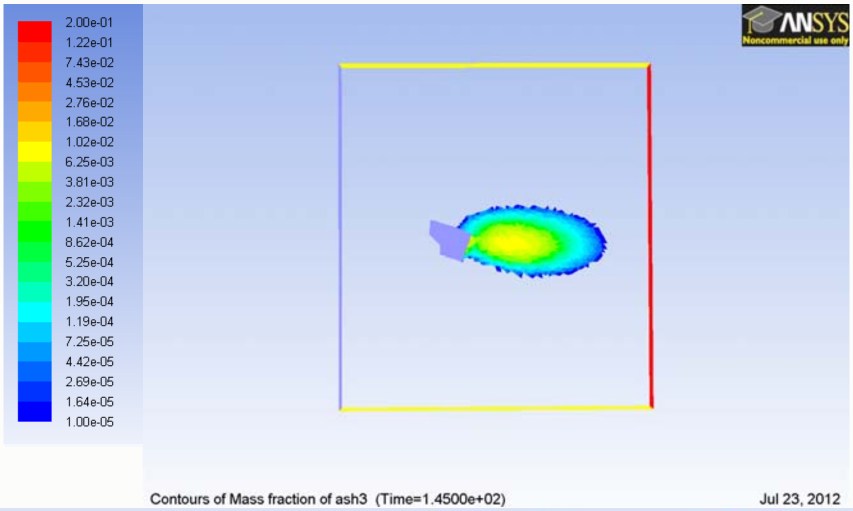

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ANSYS
Noncommercial use only
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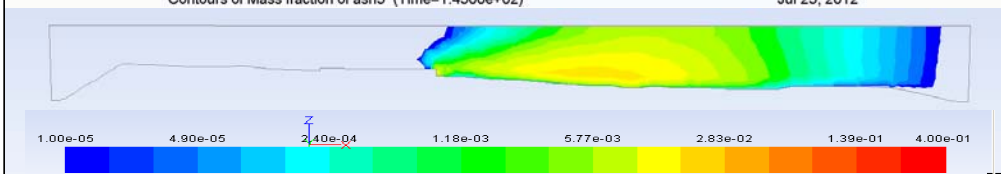
Jul 23, 2012



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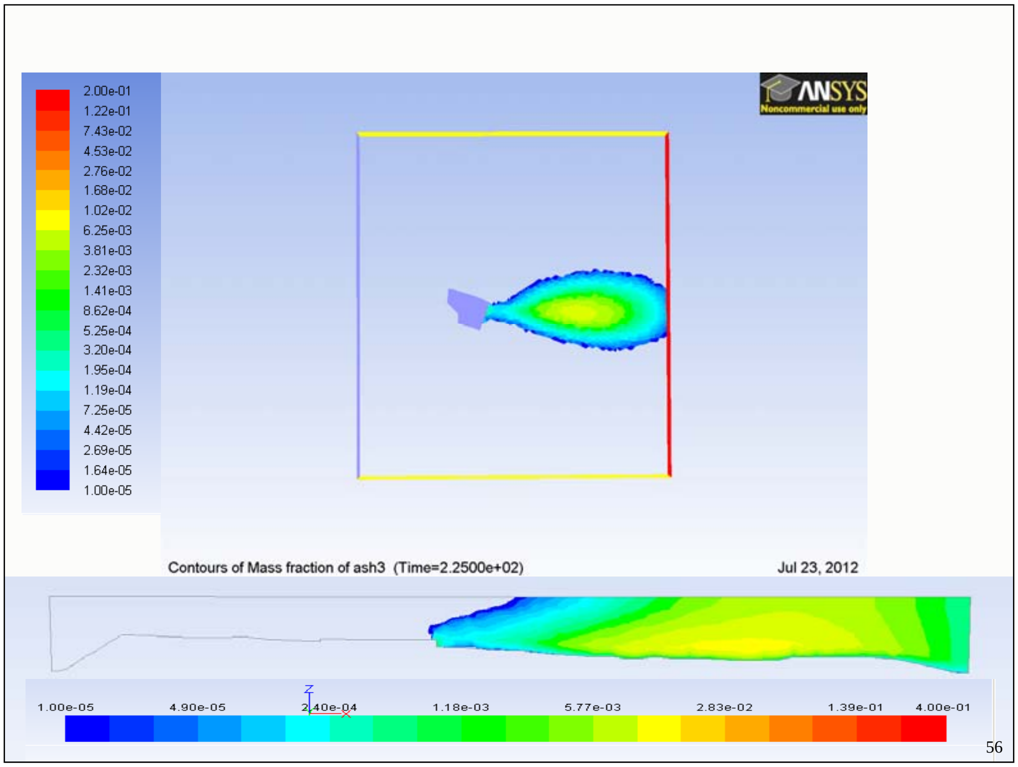
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3.81e-03
2.32e-03
1.41e-03
8.62e-04
5.25e-04
3.20e-04
1.95e-04
1.19e-04
7.25e-05
4.42e-05
2.69e-05
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ANSYS
Noncommercial use only
Contours of Mass fraction of ash3 (Time=2.2500e+02)
Jul 23, 2012
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1.18e-03
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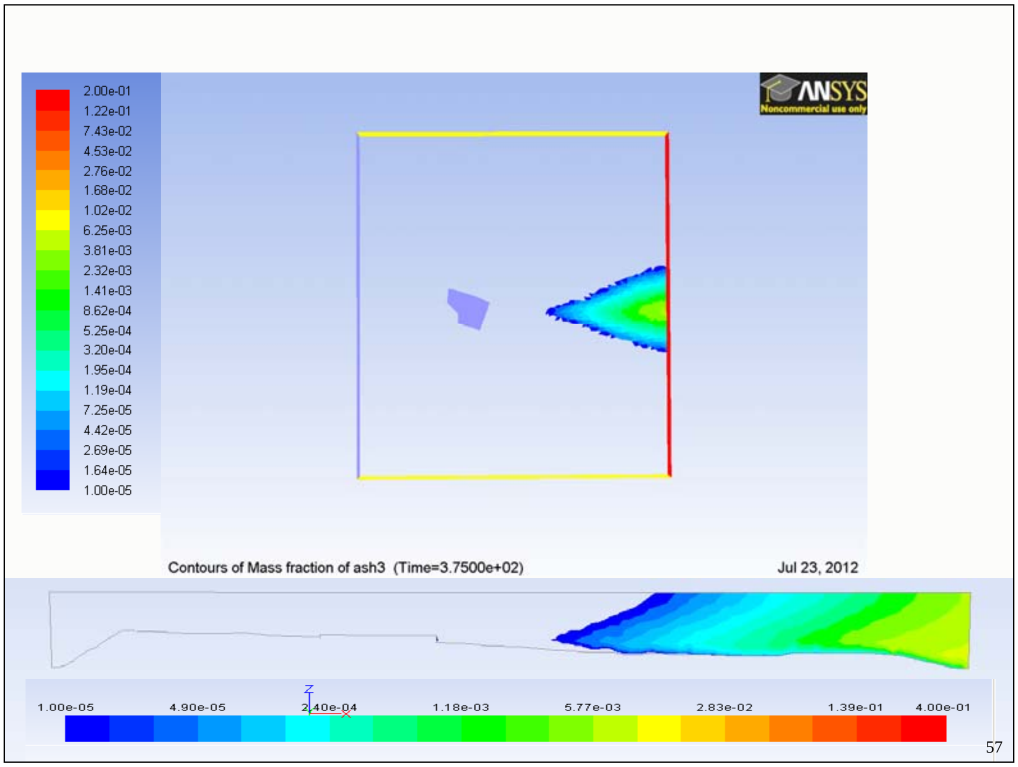

2.00e-01
1.22e-01
7.43e-02
4.53e-02
2.76e-02
1.68e-02
1.02e-02
6.25e-03
3.81e-03
2.32e-03
1.41e-03
8.62e-04
5.25e-04
3.20e-04
1.95e-04
1.19e-04
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Contours of Mass fraction of ash3 (Time=3.7500e+02)
Jul 23, 2012
1.00e-05
4.90e-05
2.40e-04
1.18e-03
5.77e-03
2.83e-02
1.39e-01
4.00e-01

Summary

- Concentrations of As and Pb near smelter sites peak in the fine particle size fraction (0.3 μm). These particles penetrate deep into the lungs. They are, in principle, collected at small efficiency (20%) but can grow due to their hygroscopic nature.
- Windblown dust from mine tailings leads to concentration of contaminants in coarse particle size range.
- Pb isotope analysis provides a "fingerprint" that may be used to provide source apportionment of contaminants.
- Preliminary results suggest that phytoremediation may lead to net decrease in contaminated dust concentrations.
- CFD can be used to assess contaminant transport from mining sources to populated areas.

Questions?

Phoenix July 5, 2011

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Epidemiologic approaches to tracking human health effects of low-level arsenic exposure

Margaret Rita Karagas
Dartmouth College, Geisel School of Medicine

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Arsenic Drinking Water Standards

World Health Organization
- 1958 – 200 ug/L
- 1963 – 50 ug/L
- 1993 – 10 ug/L

US EPA
- 2001 – 10 ug/L

Some states
- 5 ug/L

Private Wells Not Regulated

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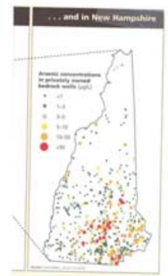
Arsenic in Private Wells in the US…New Hampshire



~40% use **private water** systems

>10% private well **As >MCL**

Largely attributed to **bedrock geology**

Overview

- Biomarker approach to studying arsenic exposure and cancer risk in a US population (>7000 participants, >3000 wells)
  - exposure biomarkers & cancer
  - gene-environment interactions
- Extending this work to examine health impacts of *in utero* and early life exposures (1000 maternal/infant pairs projected)

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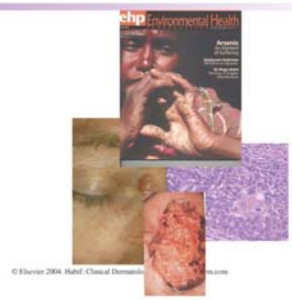
Skin Lesions & Cancer

- **Dermal lesions,** including pre-cancers: early manifestation of chronic arsenic exposure in highly exposed populations
- **Skin cancer,** especially SCC: malignancy noted in 1887 from Fowler's solution; SW Taiwan 1968
- **What about lower levels of exposure?**



- Often occur near vital structures, capable of metastasizing, can be difficult to treat
- Challenge to study in US because they not monitored

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US Population-Based Skin Cancer Case-Control Study

Design:
- Cases: state-wide surveillance
- Controls: population lists

Elevated odds ratio for SCC in highest category of toenail arsenic OR = 2.1, and evidence of a dose-related increase at higher levels of exposure

Data Collection
- Interview
- Samples
  - Water
  - Blood/buccal
  - Toenails
  - Tumor

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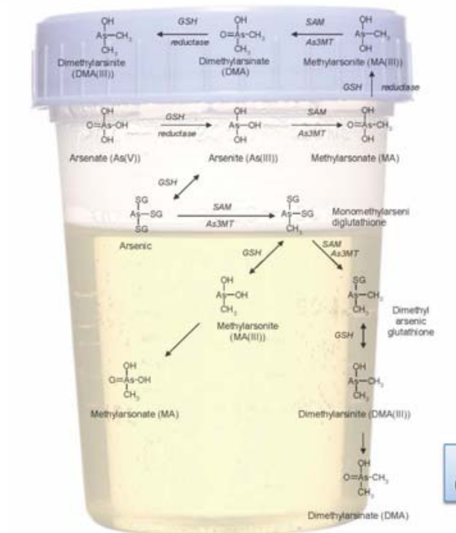

Urinary Arsenic Metabolism

iAs3 ↦ iAs5 ↦ MA ↦ DMA

Total* = Σ

**excludes arsenobetaine*

ICP-MS sensitive approach
0.10 to 0.15 ug/L for individual species

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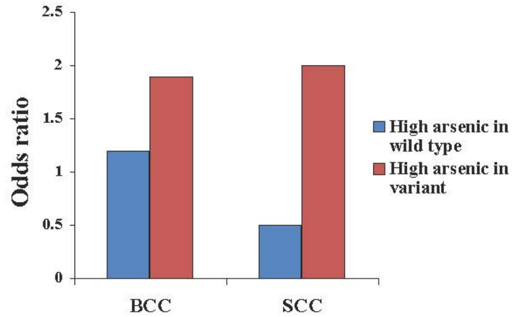
Individual Susceptibility

Greater risks of BCC and SCC among those with high arsenic & variant XPD 751 genotype



Applebaum, Nelson et al., 2007 EHP

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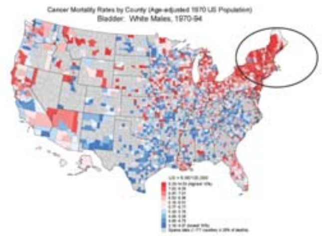
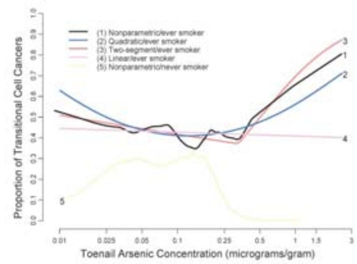
Bladder Cancer



High bladder cancer mortality rates in NH

Dose-response: relation with toenail As among smokers



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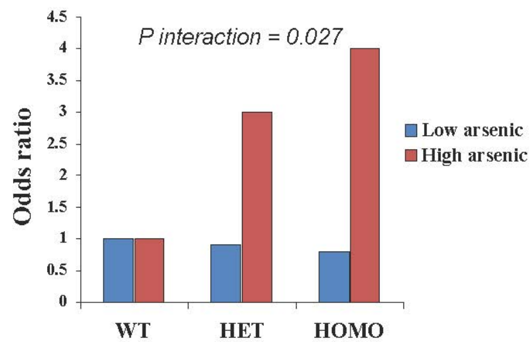
Genome-Wide Study, Validated in Bladder Cancer Case-Control Study

As-*SLC39A2* interaction, especially among smokers



Karagas et al., Human Genetics, 2012

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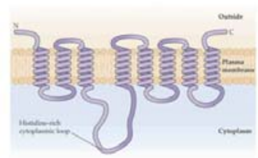
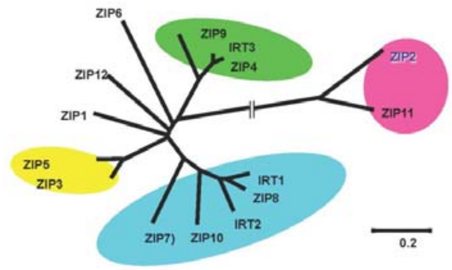
SLC39A: ZIP2 - ZIP family of metal transporters

- *ZIP* family members are metal transporters found in a wide range of organisms
- *ZRT - IRT* related Proteins
  - ZRTs – zinc regulated transporters
  - IRTs, major iron transporters
- Not known to transport As
- As replaces zinc in protein motifs i.e., tumor suppressors





Susceptible Populations

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Arsenic passes through the placenta

Concordance between maternal-cord blood concentrations

- In an Andean population: median arsenic levels in maternal blood (11 ug/L) were nearly as high in infant cord blood (9 ug/L); placental tissue also elevated (Concha et al, 1998)
- In Bangladesh, maternal-cord blood highly correlated for total arsenic (r= 0.93), MMA (r=0.80), DMA (r=0.94), As+3 (r=0.80), As+5 (r=0.89) (Hall et al., 2007)

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In Utero/early life exposures and cancer risk

- Animal experiments found maternal arsenic exposure during pregnancy led to cancers in the offspring (*Waalkes et al., 2004*)

- Antofagasta Chile found increased mortality risks of lung and liver cancer among those with born around the time of peak exposure (*Smith et al., 2006; Liaw et al., 2008*)

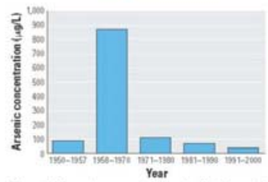

Figure 1. Arsenic concentrations in Antofagasta/Mejillones water by year. An arsenic removal plant was installed in 1971.

Thailand Study

- Women receiving prenatal care in an area with arsenic-containing drinking water (n=32 maternal/infant pairs)
- Microarray analysis of cord blood samples & toenail arsenic (<>0.5ug/g)
- Identified altered gene expression in
  - Tumor promoter, progression
  - Immune response pathways.

Fry et al., PLoS Genetics, 2007

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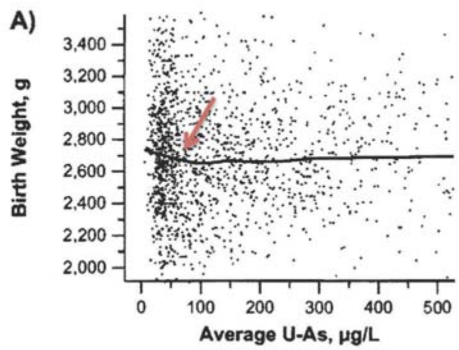
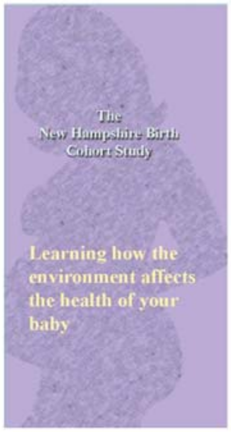
Arsenic & Birth weight



Decreased birth weight < 100 ug/L urinary As of 1. 7 g per ug/L

No data on these outcomes in a US population

Rahman et al., 2009



Study Goals

To test the hypothesis that prenatal exposure to arsenic is associated with reduced birth weight, fetal growth and gestational age (i.e., premature births) in New Hampshire.

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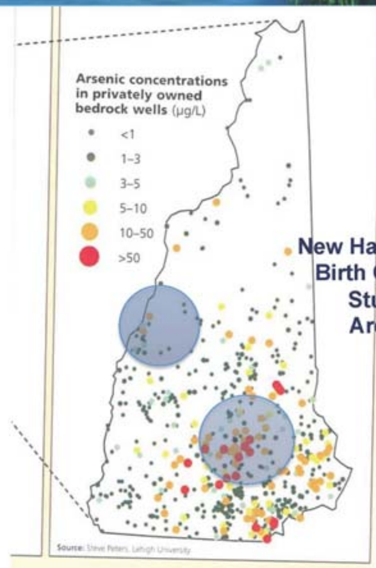
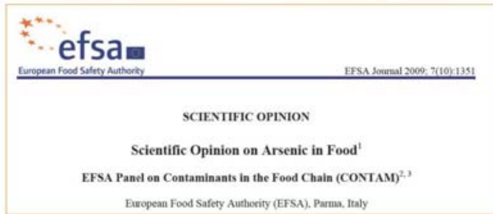
Water: an important exposure route

15-20% of pregnant women enrolled in our study – tap water exceeds the MCL of 10 ug/L As



Dietary Sources of Arsenic


efsa
European Food Safety Authority
EFSA Journal 2009; 7(10):1351

SCIENTIFIC OPINION

Scientific Opinion on Arsenic in Food[1]

EFSA Panel on Contaminants in the Food Chain (CONTAM)[2, 3]

European Food Safety Authority (EFSA), Parma, Italy

Conclusions:

Adult intake 0.13 – 0.56 ug/kg of body weight

Children < 3 yrs is 2-3 x higher than adults

Diet is the main source of exposure

BMD01 0.3 – 8 ug/kg of body weight

"Dietary exposure to arsenic should be reduced"

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New Hampshire Birth Cohort Study

Pregnancy → **Delivery** → **Months 4-8** → **Year 1**

Pregnancy

<u>12-16 Weeks</u>
Eligibility screen

<u>24-28 Weeks</u>
Enrollment
- Questionnaire
- Maternal blood, urine, hair, toenail

Maternal diet (FFQ, diary)
Prenatal records: Maternal Infection

Delivery

- Gest. age,
- birth weight

- Maternal/infant infection
- Placenta (gene expression)
- Cord blood (immune profile, epigenetics)
- Meconium
- Neurobehavioral assessment

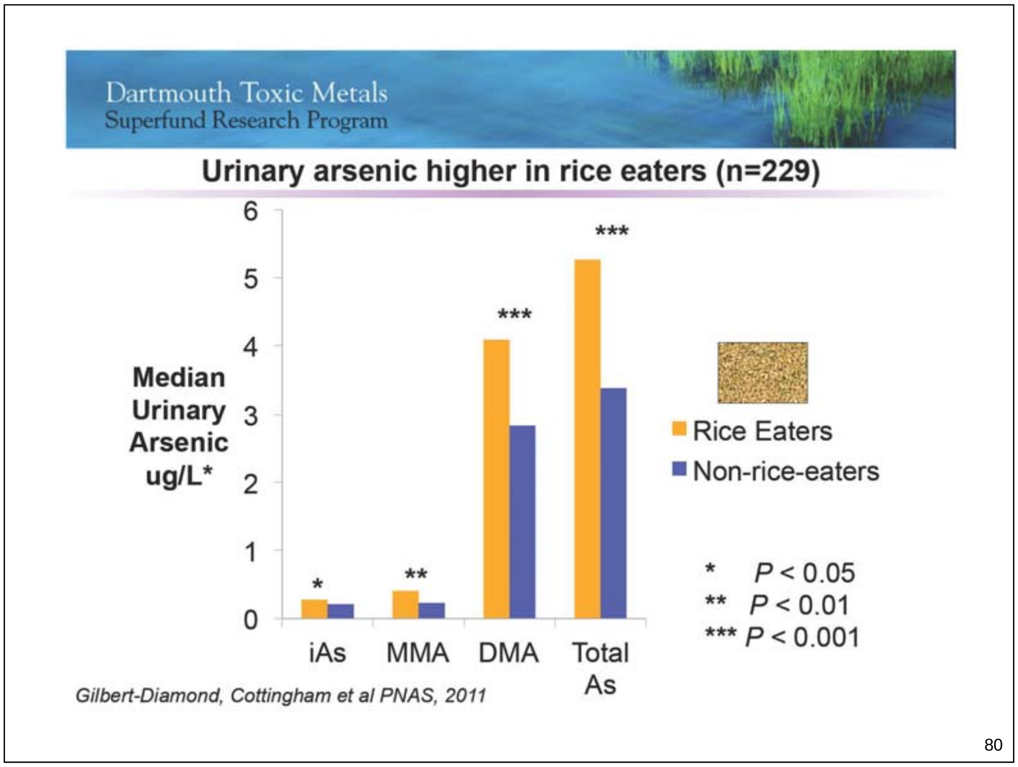
Months 4-8

- Infant infection
- Infant Diet
- Infant Urine/ Stool, Breast Milk

Year 1

- Infant health/
- infection
- Infant/ Maternal diet(FFQ)*
- Pediatric record
- Infant Blood/ Urine/ Stool

75-80% participation ~100% urinary As, water/diet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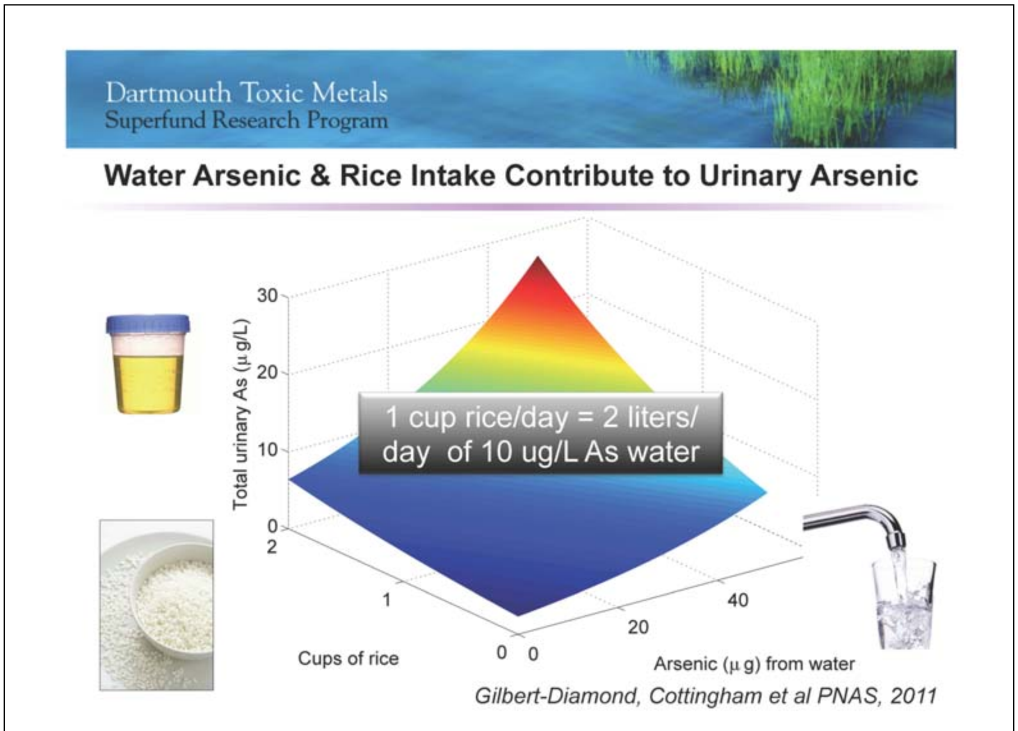
Urinary arsenic higher in rice eaters (n=229)
Median Urinary Arsenic ug/L*
6
5
4
3
2
1
0
*
**
***
***
iAs
MMA
DMA
Total As
Rice Eaters
Non-rice-eaters
* P < 0.05
** P < 0.01
*** P < 0.001
Gilbert-Diamond, Cottingham et al PNAS, 2011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Water Arsenic & Rice Intake Contribute to Urinary Arsenic
1 cup rice/day = 2 liters/ day of 10 ug/L As water
Total urinary As (μg/L)
30
20
10
0
2
1
0
Cups of rice
0
20
40
Arsenic (μg) from water
Gilbert-Diamond, Cottingham et al PNAS, 2011

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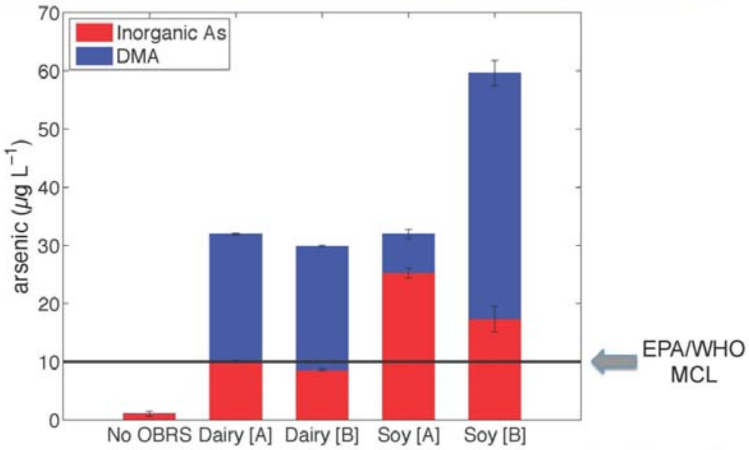
Formulas with organic brown rice syrup contained As when reconstituted with As-free water



Jackson et al., *EHP, 2012*

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Rice Consumption and Urinary Arsenic Concentration in US Children

nhanes National Health and Nutrition Examination Survey

Panels
2003-04
2005-06
2007-08

→ 
2,323 US children (ages 6 to 17 years)

Linked USDA food code

Food Commodity Intake Database
grams dry rice/USDA food code

→ Urinary Arsenic Concentration

24 hours

Davis et al, EHP, 2012

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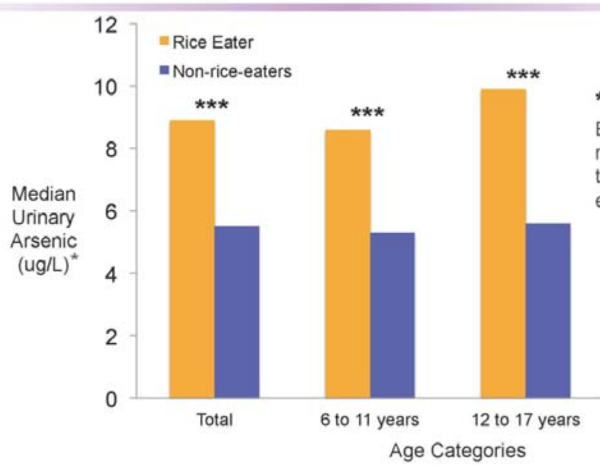
Rice Consumption and Urinary Arsenic Concentration in US Children



*** $P < 0.001$
Based on adjusted models & restricted to non-seafood-eaters

**excludes arsenobetaine & arsenocholine*

Davis et al, EHP, 2012

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Studies characterizing dose-response at low level arsenic exposures

Endpoint	Population	Reference point µg/L water	Reference point µg/kg b.w. per day
Dermal lesions	Bangladesh (Ahsan et al., 2006)	$BMCL_{01}$: 23[a]	$BMDL_{01}$: 2.2-5.7[b]
Dermal lesions	Bangladesh (Rahman et al., 2006a)	$BMCL_{01}$: 5[a]	$BMDL_{01}$: 1.2-4.1[b]
Dermal lesions	Mongolia (Xia et al., 2009)	$BMCL_{01}$: 0.3[a]	$BMDL_{01}$: 0.93-3.7[b]
Lung cancer	Chile (Ferreccio et al., 2000)	$BMCL_{01}$: 14 (NRC, 2001)	$BMDL_{01}$: 0.34-0.69[c]
Bladder cancer	North East Taiwan (Chiou et al., 2001)	$BMCL_{01}$: 42 (NRC, 2001)	$BMDL_{01}$: 3.2-7.5[b]
Skin cancer	USA (New Hampshire) (Karagas et al., 2002)	Change point[d]: 1-2	Change point: 0.16-0.31[c]
Bladder cancer	USA (New Hampshire) (Karagas et al., 2004)	Change point: *ca.* 50	Change point: 0.9-1.7[c]

Benchmark response of 1% excess risk, lower 95% confidence interval per ug/kg body weight 0.3 to 8 ug/kw body weight, EFSA 2009

Future Directions

"… infectious diseases remain a significant cause of mortality worldwide, and indeed prompted the installation of the wells in Bangladesh as a means of supplying pathogen-free drinking water. Recent evidence suggests that environmental toxins, such as arsenic, might affect immune response. Thus far, the repercussions of arsenic exposure on the occurrence and virulence of infectious diseases have not been realised entirely."

Karagas MR. Lancet 2010

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Dartmouth

Angeline Andrew, Brock Christensen,
Kathy Cottingham, Matt Davis,
Diane Gilbert-Diamond,
Eugene Demidenko,
Mary Lou Guerinot,
John Heaney, Brian Jackson,
Zhongze Li, Carmen Marsit,
Jason Moore, Ann Perry,
Tracy Punshon, Vicki Sayarath,
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Arizona
Jay Gandolfi
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Kari Nadeau
UNC
Rebecca Fry
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Miami
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THE CHILDREN'S ENVIRONMENTAL HEALTH AND DISEASE PREVENTION CENTER AT DARTMOUTH

DARTMOUTH COLLEGE, HANOVER, NEW HAMPSHIRE

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